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MINIREVIEW

Someone like it hot? Effects of global warming on insect immunity and microbiota

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Abstract

Global warming represents a substantial challenge on a broad range of organisms with diverse life-history traits and geographical distributions. Up till now several studies correlated global warming to changes in body mass, growth rate or fat content, whereas the effects on immune function and microbiota composition remained almost unexplored. On the contrary, some pioneering studies are showing that increased temperature may influence the insect immune function and the microbiota composition, making global warming in a pivotal position influencing insect survival and adaptation to a warming planet.

Key Words: global warming; immunity; microbiota composition; thermal tolerance; symbionts

Living in a warming planet

Temperature is considered one of the most important ecological factors for ectothermic organisms and the ability to tolerate temperature fluctuations is essential for individual survival (Overgaard and Sørensen, 2008). Consequently, global warming may pose a substantial challenge on many natural systems and in particular for tropical ectotherms, living close to their upper critical thermal limits, making them particularly vulnerable to global warming (Sala *et al.,* 2000; Thomas *et al.,* 2004).

Insects are among the groups of organisms most likely to be affected by climatic changes because climate has direct influences on their development, reproduction and survival (Bale *et al*., 2002; Savage *et al*., 2004; Frazier *et al*., 2006; Menéndez, 2007). Nevertheless, insects have short generation times and high reproductive rates, so that they can respond quicker to climate change than long-lived organisms, such as plants and vertebrates (Bale *et al*., 2002; Menéndez, 2007). Warming can therefore potentially affect several aspects of insect life-cycle and ecology, and potential responses could include changes in phenological patterns and habitat selection and the expansion/contraction of geographic and altitudinal ranges (Bale *et al*., 2002; Menéndez, 2007; Berg *et al*., 2010).

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Global average surface temperature increased by about 0.6 ºC during the past century, and the third IPCC report predicts that temperatures will continue to rise during the next century, with increases of up to 5.8 ºC by the year 2100 (Houghton *et al*., 2001). The study of how these human-induced changes in climate may affect biodiversity has attracted a vast research effort during the last two decades in order to study the ecological impacts of current warming on a broad range of organisms with diverse life-history traits and geographical distributions (Menéndez, 2007).

Due to the importance of insects for human health and activities (such as agriculture), several studies focused their attention on insects showing that in temperate regions, climate warming is predicted to benefit many insect species since less severe winter months could results in higher over-wintering survival and increase in the population sizes (Bale *et al*., 2002; Botkin *et al*., 2007). Moreover, climate warming could lengthen the growing season resulting in increased growth, reproduction rate and number of generations per year. The effects could be hampered in cool climate zones, where climate warming could increase insect fitness by bringing them closer to their physiological optima (Bale *et al*., 2002; Botkin *et al*., 2007). Is therefore global warming always beneficial for insects? What could happen to tropical insects that already live close to their optimal temperature? Can climate warming decrease their fitness by exceeding the physiological optima?

Aphids, for instance, are not always able to adapt physiologically to high temperatures since

they are already living close to their upper temperature limit for survival (Neve *et al*., 2009; Hazel *et al*., 2010). As reported by Chiu *et al.* (2012), global warming seems to affect the fitness of the aphid *Myzus varians* altering several physiological functions, including immunity, development and reproduction. In particular, more than 90% of *M. varians* nymphs reached adulthood in the temperature regimes with a daily mean temperature of 28.8 and 30.0 °C, whereas no nymphs reached adulthood at 32.5 °C. At the same time, the mean fecundity of aphids reared at 28.8 °C was greater than that for aphids reared at 30.0 °C, showing that even a small increase in mean temperature from 28.8 to 30.0 °C could cause a decline in the fitness of *M. varians* so that aphid populations could go extinct locally and populations will not rebound even when temperatures become favourable in the fall (Chiu *et al.,* 2012).

Up till now several studies correlated global warming to changes in some aspects, such as body mass, growth rate or fat content as fitness-related parameters (Bale *et al*., 2002; Botkin *et al*., 2007), whereas the effects on immune function and microbiota composition remained almost unexplored. In view of this assumption the present paper has been focussed mainly on the effects of warming on insect immune function and microbiota composition, parameters that could play important roles in insect survival and adaptation to a warming planet.

Fig. 1 Global warming can positively influence immunity (by enhancing the activity of some molecules), reproduction (favouring increased egg deposition, faster grow and over-wintering survival) and resource availability (for instance by making faster grow plants). However, global warming also induces heat stress that has costs that could reduce the resources available for reproduction and immune responses.

Insect immunity and global warming

Insects present an immune system endowed with only innate immune components consisting of cellular and humoral factors (Mandrioli *et al*., 2003; Nappi *et al*., 2004; Malagoli *et al*., 2007, 2010). Cell-mediated immunity includes phagocytosis and encapsulation, exerted by specific cell types (Ballarin *et al*., 2008), while humoral mediators comprise several factors among which the antimicrobial peptides (AMPs) and the components of the pro-phenoloxidase (pro-PO) cascade have been the most elucidated (Bulet and Stöcklin, 2005). It is important to observe that cellular and humoral components have not to be considered as separate elements, because several findings indicated that secreted factors are fundamental for clotting and pathogen recognition and engulfment (Bulet and Stöcklin, 2005).

The maintenance and deployment of an efficient immune response may shift away resources from other functions (such as reproduction), so that immune function results from physiological trade-offs in insects (Bonneaud *et al*., 2003; Schmid-Hempel, 2003, 2005; Rolff *et al*., 2004). In view of its cost, the immune response is influenced therefore by both biotic and abiotic factors (such as food availability and temperature) (Le Moullac and Haffner, 2000; Mydlarz *et al*., 2006; De Block and Stoks, 2008; Karl *et al*., 2011). According to these assumptions, the predicted increase in thermal stress due to global warming (Diffenbaugh *et al*., 2005, 2007) is likely to induce cascading effects on other functions such as the immune response, thus further reducing the individual fitness and favouring the distribution and prevalence of infectious diseases (Lafferty, 2009; Travers *et al*., 2009).

In order to verify this hypothesis, Karl *et al.* (2011) investigated in the tropical butterfly *Bicyclus anynana* the effects of temperature changes on fitness-related adult traits (such as body mass and fat content) and on phenoloxidase (PO) activity and hemocyte numbers that are two key parameters for evaluating the immune function at both cellular and humoral levels. Interestingly, results on body mass and fat content suggest that global warming could be beneficial, whereas haemocyte numbers and PO activity decreased at increasing temperatures (Karl *et al.,* 2011) supporting the hypothesis that immune parameters were negatively affected by global warming. At higher temperatures, insects may therefore increase their rate of growth and reproduction, but may become more susceptible to diseases, leading to reduced lifespan and possibly reduced fitness in the field (Figure 1).

At the same time, Karl *et al*. (2011) observed that the decrease in PO activity with increasing temperature was more evident in food-deprived individuals, in respect to butterflies having access to food showing a trade-off relating energy shortage and immune response. Even if the molecular mechanism at the basis of this change in the PO activity has not been studied, a direct link between the expression of heat shock proteins and a decrease in immune parameters could be

suggested. Interestingly, two mediators of the response to stress (norepinephrine and glucocorticoids) are known in mammals to act as immune-suppressors thus decreasing disease resistance (Sternberg, 2006).

The study of the trade-off between immune response and thermal tolerance is absolutely relevant in medicine and agriculture since if both immune function and reproduction are simultaneously enhanced, then climate change will result in the reproduction of more insects that will be more resistant to diseases. As a consequence, we will have more pest crop insects in our fields with more damages for agriculture, together with larger numbers of insects relevant for the transmission of human diseases. On the contrary, if higher temperatures induce or exacerbate trade-offs between reproduction and immune function, in order to face the global warming insects have to define if put their resources mainly on reproduction or on the immune systems.

A possible reply to this question can be obtained from studies performed in the cricket *Gryllus texensis*, where empirical evidence suggested that warmer temperatures lead to a decline in some immune functions (e.g. melanisation) (Suwanchaichanda and Paskewitz, 1998; Adamo and Lovett, 2004). In particular, it emerged that *G. texensis* may become more susceptible to some pathogens at higher temperatures suggesting that reproductive rate and immune function are not simultaneously enhanced at higher temperatures.

A further confirmation of the presence of a strict trade-off between immune response, reproduction and temperature has been observed by an interesting set of data published by Adamo and Lovett in 2004. In particular they reported that elevated temperatures resulted in increased egg laying, faster egg development and greater mass gain in *Gryllus texensis*. In the same experiments a reduction in the resistance to the Gram-positive bacterium *Bacillus cereus* was observed both above or below the average field temperature (26°C) suggesting that increased temperatures induce trade-offs between reproduction and disease resistance for some species–pathogen interactions (Adamo and Lovett, 2004). Interestingly, these results also explain the choice of ecological niches by *G. texensis* that prefers temperatures lower than those corresponding to the optimal reproductive output, but that assure the presence of an efficient immune response.

The ecological immunity could suffer global warming

Bacteria commonly interact with insects in intimate associations known as symbioses, where symbionts increase host fitness (for a review see Russell and Moran, 2006). Several evidences suggested that symbiotic bacteria present in the insect gut resulted to be involved not only in the degradation of specific substances in the food (Brummel *et al*., 2004), but also in other complex interactions protecting the host from invasion by pathogenic microorganisms (a process known as “colonization resistance”) and modulating the insect immune system (Dillon and Charnley, 1996; Ryu *et al*., 2008).

Microbiota seems therefore to act in insects (and actually not only in insects) as a sort of ecological immunity or extended immune system being able of affecting the efficiency of the host immune system and limiting the accumulation of pathobionts (Ottaviani *et al*., 2012).

According to this proposal, germ-free locusts died prematurely due to infection of pathogens, such as *Pseudomonas aeruginosa*, *Penicillium* spp. and *Bacillus subtilis* (Charnley *et al.,* 1995; Dillon and Charnley, 1996, 2005), suggesting that they are more susceptible to infection than normal insects and that the gut microbiota exerted a protective function out-competing potentially harmful organisms (Dillon *et al*., 2005). The involvement of microbiota in the host immune protection can vary during insect life, since the composition of the bacterial community that populates the insect gut is not stable, but can change during lifespan due to variation in the nutritional composition of the food and the aging process (DeVeale *et al.,* 2004).

In a recent paper, Chiu *et al.* (2012) reported a low survival of nymphs of the aphid *M. varians* at high temperatures as a consequence of the elimination of endosymbionts, such as *Buchnera* (as previously suggested by Ohtaka and Ishikawa, 1991). This effect probably results from a temperature-mediated decrease in aphid endosymbionts, which synthesize amino acids essential for their insect hosts (Chen *et al*., 2009).

In the last years, different roles have been suggested for symbionts other than the synthesis of amino acids only (Russell and Moran, 2006). *Buchnera* might, for instance, play a key role in aphid thermal tolerance since endosymbionts code for heat shock proteins, which deter degradation of host protein secondary structure (Dunbar *et al*., 2007). Secondary endosymbionts, such as *Serratia simbiotica*, play a similar role in the thermal tolerance of their host strengthening the ability of aphids to evolve further adaptations to overcome the impacts of warming (Russell and Moran, 2006).

Buchnera are at least partly able to survive at high temperatures because of constitutive expression of genes that are normally up-regulated in response to heat and aphids could be able to thrive under temperatures as high as 35°C in the laboratory (Dunbar *et al*., 2007). Surprisingly, a single nucleotide deletion in the *Buchnera ibpA* gene encoding for a small heat-shock protein virtually eliminates the transcriptional response of *ibpA* to heat stress and lowers its expression even at cool or moderate temperatures (Dunbar *et al*., 2007). In the presence of this mutant allele, a short heat exposure in juveniles has strong effects on aphids that produce few or no progeny and contain almost no *Buchnera,* in contrast to aphids bearing symbionts without the deletion.

The *ibpA* mutated allele has appreciable frequencies in field populations supporting the view that lowering of *ibpA* expression improves host fitness under some conditions (Dunbar *et al*., 2007).

As previously suggested, the response to stress (including thermal stress) is part of a large trade-off that relates stress response to reproduction and immunity. This mutation by switching off the response to heat stimuli could favor aphid reproduction and immunity. However, the prolonged permanence of aphids at high temperatures (for instance in hot summer with daily mean temperature of 32.5 °C) results in the elimination of *Buchnera* reducing not only the thermal tolerance of aphids, but also their fecundity since the lack of endosymbionts results in a lost synthesis of amino acids essential for the hosts (Chiu *et al*., 2012).

According to these results, global warming could be difficultly faced by aphids in tropical regions due to *Buchnera* symbiont depletion. Interestingly, in the presence of low density of primary symbionts, secondary symbionts (such as *Hamiltonella defensa*, *S. symbiotica, Regiella insecticola*) could be more present affecting not only the aphid thermal tolerance to high temperatures, but also their symbiont-based immune response (Poirié and Coustau, 2011).

The effects of global warming on the composition of aphid microbiota are of particular interest since, as recently reviewed by Poirié and Coustau (2011), the immune deficiency (IMD) signalling pathway was apparently non functional in aphids and no genes coding for peptidoglycan recognition proteins (PGRPs) and several well-conserved antimicrobial peptides, such as defensins and cecropins, have been predicted in the pea aphid *Acyrthosiphon pisum* genome (Gerardo *et al*., 2010), making the microbiota-based immunity essential to protect the host against natural enemies (Poirié and Coustau, 2011).

Global warming: threat or opportunity?

Global warming is a well-studied phenomenon referring to the current temperature of Earth's atmosphere and oceans and it is responsible for climate-driven habitat changes that could influence insect survival and distribution. According to some proposals, the predicted increase in the Earth temperature could benefit many insect species since they will face less severe winter months resulting in higher over-wintering survival and increase in the population sizes. Moreover, climate warming could lengthen the growing season resulting in increased growth, reproduction rate and number of generations per year. Even if these hypotheses are intriguing, the scenario could be more complex in view of the existence of different trade-offs that balance the cost of reproduction and stress and immune responses. As suggested by some pioneering studies, global warming could have detrimental effects not only on insect immune system, but also on the composition of their microbiota making insects more vulnerable to pathogens. The occurrence of increasing temperature could therefore exacerbate the trade-offs between reproduction and immune function, making few resources available for disease resistance.

The study of trade-offs related to global warming has an important value not only from a biological point of view, but also at an ecological level. Indeed, in order to balance the use of resource, several insect species that at present live in tropical regions will shift to temperate areas of our planet in order to combine a successful reproductive output to the an efficient immune response suggesting a huge impact of global warming on biodiversity.

References

Adamo SA, Lovett MME. Some like it hot: the effects of climate change on reproduction, immune function and disease resistance in the cricket *Gryllus texensis*. J. Exp. Biol. 214: 1997-2003, 2004.

Bale JS, Masters GJ, Hodkinson ID, Awmack C, Bezemer TM, Brown VK, *et al*. Herbivory in global climate change research: direct effect of rising temperature on insect herbivores. Global Change Biol. 8: 1-16, 2002.

Ballarin L, Cammarata M, Cima F, Grimaldi A, Lorenzon S, Malagoli D, *et al.* Immune-neuroendocrine biology of invertebrates: a collection of methods. Inv. Surv. J. 5: 192-215, 2008.

Berg MP, Kiers ET, Driessen G, van der Heijden M, Kooi BW *et al.* Adapt or disperse: understanding species persistence in a changing world. Global Change Biol. 16: 587-598, 2010.

Bonneaud C, Mazuc J, Gonzalez G, Haussy C, Chastel O, Faivre B, *et al*. Assessing the cost of mounting an immune response. Am. Nat. 161: 367-379, 2003.

Botkin DB, Saxe H, Araújo MB, Betts R, Bradshaw RHW, *et al.* Forecasting the effects of global warming on biodiversity. BioScience 57: 227-236, 2007.

Brummel T, Ching A, Seroude L, Simon AF, Benzer S. *Drosophila* lifespan enhancement by exogenous bacteria. Proc. Natl. Acad. Sci. USA 101:12974-12979, 2004.

Bulet P, Stöcklin, R. Insect antimicrobial peptides: structures, properties and gene regulation. Protein Pept. Lett. 12: 3-11, 2005.

Charnley AK, Hunt J, Dillon AR. The germ-free culture of desert locusts, *Schistocerca gregaria*. J. Insect Physiol. 31:477-485, 1995.

Chen B, Zhong D, Monteiro A. Comparative genomics and evolution of the HSP90 family of genes across all kingdoms of organisms. BMC Genomics 7: 156, 2009.

Chiu MC, Chen YH, Kuo MH. The effect of experimental warming on a low-latitude aphid, *Myzus varians*. Entomol. Exp. Appl. 142: 216-222, 2012.

De Block M, Slos S, Johansson F, Stoks R. Integrating life history and physiology to understand latitudinal size variation in a damselfly. Ecography 31: 115-123, 2008.

DeVeale B, Brummel T, Seroude L. Immunity and aging: the enemy within? Aging Cell 3: 195-208, 2004.

Diffenbaugh NS, Pal JS, Trapp RJ, Giorgi F. Fine-scale processes regulate the response of extreme events to global climate change. Proc. Nat. Acad. Sci. USA 102: 15774-15778, 2005.

Diffenbaugh NS, Pal JS, Giorgi F, Gao X. Heat stress intensification in the Mediterranean climate change hotspot. Geophys. Res. Lett. 34: L11706, 2007.

Dillon R, Charnley AK. Colonization of the guts of germ-free desert locusts, *Schistocerca gregaria*, by the bacterium *Pantoea agglomerans*. J. Invertebr. Pathol. 67: 11-14, 1996.

Dillon R, Charnley K. Mutualism between the desert locust *Schistocerca gregaria* and its gut microbiota. Res. Microbiol. 153: 503-509, 2005.

Dunbar HE, Wilson ACC, Ferguson NR, Moran NA. Aphid thermal tolerance is governed by a point mutation in bacterial symbionts. PLoS Biol. 5: e96, 2007.

Frazier M, Huey R, Berrigan D. Thermodynamics constrains the evolution of insect population growth rates: "Warmer is better". Am. Nat. 168: 512–520, 2006.

Gerardo NM, Altincicek B, Anselme C, Atamian H, Barribeau SM, de Vos M, *et al*. Immunity and other defenses in pea aphids, *Acyrthosiphon pisum*. Genome Biol. 11: R21, 2010.

Guinnee MA, Moore J. The effect of parasitism on host fecundity is dependent on temperature in a cockroach-acanthocephalan system. J. Parasitol. 90: 673-677, 2004.

Hazell SP, Groutides C, Neve BP, Blackburn TM, Bale JS. A comparison of low temperature tolerance traits between closely related aphids from the tropics, temperate zone, and Arctic. J. Insect Physiol. 56: 115-122, 2010.

Houghton JT, Ding Y, Griggs DJ, Noguer M, van der Linden PJ, Xiaosu D, *et al*. Climate change 2001: The scientific basis, Cambridge University Press, Cambridge, 2001.

Karl L, Stokcs I, De Block M, Janowitz SA, Fischer K. Temperature extremes and butterfly fitness: conflicting evidence from life history and immune function. Global Change Biol. 17: 676-687, 2011.

Lafferty KD. The ecology of climate change and infectious diseases. Ecology 90: 888-900, 2009.

Le Moullac G, Haffner P. Environmental factors affecting immune responses in *Crustacea*. Aquaculture 191: 121-131, 2000.

Malagoli D, Conklin D, Sacchi S, Mandrioli M, Ottaviani E. A putative helical cytokine functioning in innate immune signalling in *Drosophila melanogaste*r. Biochim. Biophys. Acta 1770: 974-978, 2007.

Malagoli D, Sacchi S, Ottaviani E. Lectins and cytokines in celomatic invertebrates: two tales with the same end. Inv. Surv. J. 7: 1-10, 2010.

Mandrioli M, Bugli S, Saltini S, Genedani S, Ottaviani E. Molecular characterization of a defensin in the IZD-MB-0503 cell line derived from immunocytes of the insect *Mamestra brassicae* (Lepidoptera). Biol. Cell 95: 53-57, 2003.

Menéndez R. How are insects responding to global warming? Tijdsch. Entomol. 150: 355-365, 2007.

Mydlarz LD, Jones LE, Harvell CD. Innate immunity, environmental drivers and disease ecology of marine and freshwater invertebrates. Annu. Rev. Ecol. Evol. Syst. 37: 251-288, 2006.

Nappi AJ, Kohler L, Mastore M. Signalling pathways implicated in the cellular innate immune responses of *Drosophila*. Inv. Surv. J. 1: 5-33, 2004.

Neve BP, Hazell SP, Groutides C, Douglas AE, Blackburn TM, Bale JS. Hyperthermic aphids: insights into behaviour and mortality. J. Insect Physiol. 56, 123-131, 2009.

Ohtaka C, Ishikawa H. Effects of heat treatment on the symbiotic system of an aphid mycetocyte. Symbiosis 11: 19-30, 1991.

Ottaviani E, Ventura M, Mandrioli M, Candela M, Franchini A, Franceschi C. Gut microbiota as a candidate for lifespan extension: an ecological/evolutionary perspective targeted on living organisms as metaorganisms. Biogerontology 12: 599-609, 2012.

Overgaard J, Sørensen JG. Rapid thermal adaptation during field temperature variations in *Drosophila melanogaster*. Cryobiology 56: 159-162, 2008.

Poirié M, Coustau C. The evolutionary ecology of aphids' immunity. Inv. Surv. J. 8: 247-255, 2011.

Rolff J, Van de Meutter F, Stoks R. Time constraints decouple age and size at maturity and physiological traits. Am. Nat. 64: 559-565, 2004.

Russell JA, Moran NA. Costs and benefits of symbiont infection in aphids: variation among symbionts and across temperatures. Proc. R. Soc. B 273: 603-610, 2006.

Ryu JH, Kim SH, Lee HY, Bai JY, Nam YD, Bae JW, *et al*. Innate immune homeostasis by the homeobox gene *Caudal* and commensal-gut mutualism in *Drosophila*. Science 319: 777-782, 2008.

Sala OE, Chapin FS 3rd, Armesto JJ, Berlow E, Bloomfield J, Dirzo R, *et al.* Biodiversity: global biodiversity scenarios for the year 2100. Science 287: 1770-1774, 2000.

Savage VM, Gillooly JF, Brown JH, West GB, Charnov EL. Effects of body size and temperature on population growth. Am. Nat. 163: 429-441, 2004.

Schmid-Hempel P. Variation in immune defence as a question of evolutionary ecology. Proc. Royal Soc. B 270: 357-366, 2003.

Schmid-Hempel P. Evolutionary ecology of insect immune defenses. Annu. Rev. Entomol. 50: 529-551, 2005.

Sternberg EM. Neural regulation of innate immunity: a coordinated nonspecific response to pathogens. Nature Rev. Immunol. 6: 318-328, 2006.

Suwanchaichinda C, Paskewitz SM. Effects of larval nutrition, adult body size, and adult temperature on the ability *Anopheles gambiae* (Diptera:

Culicidae) to melanize sephadex beads. J. Med. Entomol. 35: 157-161, 1998.

Thomas CD, Cameron A, Green RE. Extinction risk from climate change. Nature 427: 145-148, 2004.

Travers MA, Basuyaux O, Le Goic N. Influence of temperature and spawning effort on *Haliotis tuberculata* mortalities caused by *Vibrio harveyi*: an example of emerging vibriosis linked to global warming. Global Change Biol. 15: 1365-1376, 2009.